

**In the claims:**

In the claims:

1. (Currently amended) A peptide, the amino acid sequence of which consists of at least one ~~an~~ amino acid sequence selected from the group consisting of:

YLTQPQS (SEQ ID NO. 1);  
GSLPHSL (SEQ ID NO. 2);  
TQLFPPQ (SEQ ID NO. 3);  
HSIPDNI (SEQ ID NO. 4);  
HHMPHDK (SEQ ID NO. 5);  
YTTPPSP (SEQ ID NO. 6); and  
QLPLMPR (SEQ ID NO. 7).

2. (Original) The peptide of claim 1, wherein the amino acid sequence is selected from the group consisting of:

YLTQPQS (SEQ ID NO. 1); and  
TQLFPPQ (SEQ ID NO. 3).

3. (Currently amended) A peptide up to 60 amino acids in length comprising at least one ~~an~~ amino acid sequence selected from the group consisting of:

YLTQPQS (SEQ ID NO. 1);  
GSLPHSL (SEQ ID NO. 2);  
TQLFPPQ (SEQ ID NO. 3);  
HSIPDNI (SEQ ID NO. 4);  
HHMPHDK (SEQ ID NO. 5);  
YTTPPSP (SEQ ID NO. 6); and  
QLPLMPR (SEQ ID NO. 7),

wherein the peptide is capable of binding to Nogo, MAG, TNR-EGFL and/or TN-R.

4. (Original) The peptide of claim 3, which comprises the amino acid sequence YLTQPQS (SEQ ID NO. 1) or TQLFPPQ (SEQ ID

NO. 3).

5. (Currently amended) A peptide up to 60 amino acids in length comprising an amino acid sequence having at least 5 residues identical with corresponding residues in at least one ~~an~~ amino acid sequence selected from the group consisting of:

YLTQPQS (SEQ ID NO. 1);  
GSLPHSL (SEQ ID NO. 2);  
TQLFPPQ (SEQ ID NO. 3);  
HSIFDNI (SEQ ID NO. 4);  
HHMPHDK (SEQ ID NO. 5);  
YTTPPSP (SEQ ID NO. 6); and  
QLPLMPR (SEQ ID NO. 7),

wherein the peptide is capable of binding to Nogo, MAG, TNR-EGFL and/or TN-R.

6. (Original) The peptide of claim 5, which has at least 5 residues identical with corresponding residues in an amino acid sequence selected from the group consisting of:

YLTQPQS (SEQ ID NO. 1); and  
TQLFPPQ (SEQ ID NO. 3).

7. (Currently amended) The peptide of claim 5 ~~or claim 6~~, wherein the number of identical residues is at least 6.

8. (Cancelled)

9. (Currently amended) The peptide of ~~any one of claims 3 to 8~~, which is up to 40 amino acids in length.

10. (Original) The peptide of claim 9, which is up to 20 amino acids in length.

11. (Original) The peptide of claim 10, which is up to 10 amino acids in length.

12. (Currently amended) A composition for the treatment of CNS damage comprising one or more peptides according to any preceding claim 1, together with one or more pharmaceutically acceptable ingredients, said composition optionally being formulated for injection.

13. (Cancelled)

14. (Cancelled)

15. (Currently amended) A method for treating CNS damage, ~~the method in a patient in need thereof~~ comprising administering an effective amount of the composition of claim 12 ~~a peptide according to any one of claims 1 to 11 to a patient~~ at or near a site of CNS damage in the patient.

16. (Currently amended) A method as claimed in claim 15, wherein said CNS damage is selected from the group consisting of ~~for treating~~ spinal cord injury or stroke, ~~the method comprising administering to a patient a said peptide having~~ has an amino acid sequence that consists of an amino acid sequence selected from the group consisting of:  
YLTQPQS (SEQ ID NO. 1); and  
TQLFPPQ (SEQ ID NO. 3), and is administered by direct injection into a site of spinal cord injury or stroke damage in the patient.

17. (Cancelled)

18. (Currently amended) A method of designing a mimetic of a peptide as defined in ~~any one of claims 1 to 11,~~ the mimetic ~~being capable of having binding affinity for~~ to one or more of the a neuronal growth inhibitory molecules selected from the group consisting of Nogo, MAG and/or TN-R, said method

comprising:

(i) analysing a peptide ~~as defined in any one of claims 1 to 11 that is capable of binding~~ binds to one or more of said the neuronal growth inhibitory molecules Nogo, MAG and/or TN-R to determine the amino acid residues essential ~~and important~~ for the binding activity thereby ~~to define~~ defining a pharmacophore; and

(ii) modelling the pharmacophore ~~thereby to~~ designing and/or ~~screen~~ candidate mimetics, said method optionally comprising screening mimetics so designed for ~~having the~~ biological activity.

19. (Currently amended) The ~~use or~~ method of ~~claim 17 or~~ claim 18, which includes a step of assaying binding of a candidate mimetic to Nogo, MAG and/or TN-R in vitro.

20. (Currently amended) The ~~use or~~ method of ~~any one of~~ ~~claims 17 to 19,~~ claim 18 which includes a step, having identified a candidate mimetic that is capable of ~~such in~~ vitro binding said neuronal growth inhibitory molecule in vitro, of optimizing the candidate mimetic for in vivo use.

21. (Currently amended) The ~~use or~~ method of claim 20, wherein the optimized mimetic is formulated together with one or more pharmaceutically acceptable ingredients.

22. (Currently amended) A bacteriophage which expresses at least one fusion protein consisting of at least one peptide of claim 1 and a bacteriophage coat protein, such that the peptide is displayed on the surface of the bacteriophage virion, ~~wherein the peptide is as defined in any one of claims 1 to 11.~~

23. (Original) A screening method for identifying peptides capable of binding to Nogo, MAG and/or TN-R, the method

comprising:

providing bacteriophages of claim 22, ~~respectively~~  
expressing said fusion protein consisting of said at least one  
~~different~~ peptides; and

screening the bacteriophages for the ability to bind to  
Nogo, MAG and/or TN-R.

24. (Currently amended) The method of claim 23, further  
comprising wherein bacteriophages which are identified as  
being capable of binding to Nogo, MAG and/or TN-R, screening  
said bacteriophages or the peptides they display identified as  
binders, are then be screened for the ability to block the  
inhibitory effects of Nogo, MAG and/or TN-R on neuronal cell  
adhesion in an in vitro assay.

25. (Currently amended) A The method comprising all the steps  
of claim 24 further comprising and an additional step,  
following the identification of a peptide, or phage that  
displays a peptide, that is capable of blocking the inhibitory  
effects of Nogo, MAG and/or TN-R on neuronal cell adhesion in  
an in vitro assay, of formulating the peptide which blocks  
said inhibitory effects with one or more pharmaceutically  
acceptable ingredients for administration in vivo.

26. (Currently amended) A method of searching for factors ~~that~~  
~~are likely to~~ which reduce the inhibitory effect of TN-R, MAG  
and/or Nogo, the method comprising interrogating a sequence  
database to identify polypeptides, or nucleic acids that  
encode polypeptide factors, that comprise an amino acid  
sequence having at least 5 residues identical with  
corresponding residues in an amino acid sequence selected from  
the group consisting of:

YLTQPQS (SEQ ID NO. 1);

GSLPHSL (SEQ ID NO. 2);

TQLFPPQ (SEQ ID NO. 3);

HSIPDNI (SEQ ID NO. 4);  
HHMPHDK (SEQ ID NO. 5);  
YTTPPSP (SEQ ID NO. 6); and  
QLPLMPR (SEQ ID NO. 7)

said method optionally comprising screening said factors so identified for the ability to reduce the inhibitory effect of TN-R, MAG and/or Nogo on neuronal cell adhesion and formulating said inhibitory peptide factors with one or more pharmaceutically acceptable ingredients for administration in vivo.

27. (Currently amended) A method of searching for factors ~~that are likely to~~ which reduce the inhibitory effect of TN-R, MAG and/or Nogo, the method comprising screening a cDNA library with an oligonucleotide probe which is capable of hybridising under stringent conditions with a nucleic acid sequence that encodes an amino acid sequence having at least 5 residues identical with corresponding residues in an amino acid sequence selected

from the group consisting of:

YLTQPQS (SEQ ID NO. 1);  
GSLPHSL (SEQ ID NO. 2);  
TQLFPPQ (SEQ ID NO. 3);  
HSIPDNI (SEQ ID NO. 4);  
HHMPHDK (SEQ ID NO. 5);  
YTTPPSP (SEQ ID NO. 6); and

QLPLMPR (SEQ ID NO. 7) said method optionally comprising screening said factors so identified for the ability to reduce the inhibitory effect of TN-R, MAG and/or Nogo on neuronal cell adhesion and formulating said inhibitory peptide factors with one or more pharmaceutically acceptable ingredients for administration in vivo.

28. (Cancelled)

29. (Canceled)

30. (Currently amended) A nucleic acid vector ~~comprising~~  
~~nucleic acid~~ encoding one or more polypeptide domains selected  
from the group consisting of:

(a) the N-terminal domain (NogoN) of Nogo-A, or a variant  
or fragment thereof;

(b) the extracellular loop (Nogo66) of Nogo-B, or a  
variant or fragment thereof;

(c) the third to fifth immunoglobulin-like repeats of  
MAG, or a variant or fragment thereof; and

(d) the EGF-like domain of TN-R, or a variant or fragment  
thereof, wherein said fragment comprises at least 15  
contiguous amino acids from said domain, includes one or more  
epitopes of said domain and retains the ability to raise an  
antibody response in vivo, and wherein said variant includes a  
portion of at least 15 amino acids that has at least 65% amino  
acid identity to a corresponding portion of said domain.

31. (Original) The vector of claim 30, wherein the nucleic  
acid encodes at least two of the domains.

32. (Original) The vector of claim 31, wherein the domains are  
expressed as a fusion polypeptide.

33. (Original) The vector of claim 32, wherein the domains  
are separated from one another by flexible linkers.

34. (Currently amended) The vector of ~~any one of~~ claims 30 ~~to~~  
~~33~~ wherein, of the proteins Nogo A, Nogo B, TN-R and/or MAG,  
the vector is preferably capable of expressing substantially  
only the domains (a), (b), (c) and/or (d) recited in claim 30.

35. (Original) The vector of claim 34, wherein the vector is  
incapable of expressing other epitope-containing portions of

the proteins.

36. (Currently amended) The vector of claim 34 ~~or claim 35~~, wherein, of the proteins Nogo A, Nogo B, TN-R and/or MAG, the vector preferably expresses no more than 20% of the protein lying outside domains (a) to (d) recited in claim 30.

37. (Currently amended) The vector of ~~any one of claims 30 to 36~~, wherein the domain (a) has, the amino acid sequence of NogoN (1-185) (SEQ ID NO:10), domain (b) has the amino acid sequence of Nogo66 (823-888) (SEQ ID NO: 11) , domain (c) has the amino acid sequence of MAG (1-508) (SEQ ID NO:8), and domain (d) has the amino acid sequence of TNR (125-329) (SEQ ID NO:9).

38. (Original) The vector of claim 30, which encodes a polypeptide having the amino acid sequence MAG(1-508)-Ala<sub>n</sub>-TNR(125-329)Ala<sub>n</sub>-NogoN(1-185)-Ala<sub>n</sub>-Nogo66(823-888) (SEQ ID NO:12), where Ala<sub>n</sub> represents an polyalanine linker.

39. (Currently amended) A composition comprising the vector of ~~any one of claims 30 to 38~~, formulated together with one or more pharmaceutically acceptable ingredients for use as a therapeutic vaccine, said composition optionally being formulated for injection.

40. (Currently amended) A method for treating CNS damage in a patient in need thereof comprising administration of an effective amount of ~~T~~the vector of any one of claims 30 as a therapeutic vaccine ~~to 38, for use in a method of treatment.~~

41. (Currently amended) A pharmaceutical composition for the treatment of CNS damage comprising ~~Use of~~ the vector of ~~any one of claims 30~~ in a pharmaceutically acceptable carrier ~~to 38 in the manufacture of a medicament for the treatment of CNS~~



damage.

42. (Cancelled)

43. (Original) A polypeptide consisting essentially of one or more polypeptide domains as defined in claim 30.

44. (Currently amended) A ~~The polypeptide of claim 43, which is encoded by the vector of any one of claims 30-38.~~

45. (Currently amended) A composition comprising the polypeptide of claim ~~43 or claim~~ 44, formulated together with one or more pharmaceutically acceptable ingredients for use as a therapeutic vaccine.

46. (Currently amended) A method for the treatment of CNS damage in a patient in need thereof, comprising administration of an effective amount of the ~~The polypeptide of claim 43 or claim 44 composition of claim 45 to said patient, for use in a method of treatment.~~

47. (Cancelled)

48. (Cancelled)

49. (Original) An antibody capable of specifically binding to any one of domains (a)-(d) as defined in claim 37, or a mixture of antibodies together capable of binding to two, three or all four of domains (a)-(d) as defined in claim 37, for use in a method of treatment.

50. (Currently amended) A composition for the treatment of CNS damage comprising at least one ~~Use of an antibody capable of specifically binding to any one of domains (a)-(d) as defined in claim 37, or a mixture of antibodies together~~

~~capable of binding to two, three or all four of domains (a)-  
(d) as defined in claim 37, in the manufacture of a medicament  
for the treatment of CNS damage antibody of claim 49 in a  
pharmaceutically acceptable carrier, said composition  
optionally being formulated for injection.~~

51. (Currently amended) A method for treating CNS damage in a patient, the method comprising administering to the patient as a therapeutic vaccine the composition of claim 50 ~~an antibody capable of specifically binding to any one of domains (a) - (d) as defined in claim 37, or a mixture of antibodies together capable of binding to two, three or all four of domains (a) - (d) as defined in claim 37.~~

52-56 (Cancelled)

57. (New) A composition for the treatment of CNS damage comprising one or more peptides according to claim 3, together with one or more pharmaceutically acceptable ingredients, said composition optionally being formulated for injection.

58. (New) A method of designing a mimetic of a peptide as defined in claim 3, the mimetic having binding affinity for one or more of a neuronal growth inhibitory molecule selected from the group consisting of Nogo, MAG and/or TN-R, said method comprising:

(i) analysing a peptide of claim 3 that binds to one or more of said neuronal growth inhibitory molecules to determine the amino acid residues essential for the binding activity thereby defining a pharmacophore; and

(ii) modelling the pharmacophore thereby designing candidate mimetics, said method optionally comprising screening mimetics so designed for biological activity.

59. (New) A method of designing a mimetic of a peptide as

defined in claim 5, the mimetic having binding affinity for one or more of a neuronal growth inhibitory molecule selected from the group consisting of Nogo, MAG and/or TN-R, said method comprising:

(i) analysing a peptide of claim 5 that binds to one or more of said neuronal growth inhibitory molecules to determine the amino acid residues essential for the binding activity thereby defining a pharmacophore; and

(ii) modelling the pharmacophore thereby designing candidate mimetics, said method optionally comprising screening mimetics so designed for biological activity.

60. (New) A bacteriophage which expresses at least one fusion protein consisting of at least one peptide of claim 3 and a bacteriophage coat protein, such that the peptide is displayed on the surface of the bacteriophage virion.

61. (New) A bacteriophage which expresses at least one fusion protein consisting of at least one peptide of claim 5 and a bacteriophage coat protein, such that the peptide is displayed on the surface of the bacteriophage virion.

62. (New) A screening method for identifying peptides capable of binding to Nogo, MAG and/or TN-R, the method comprising:

providing bacteriophages of claim 60, expressing said fusion protein consisting of said at least one peptide; and  
screening the bacteriophages for the ability to bind to Nogo, MAG and/or TN-R.

63. (New) A screening method for identifying peptides capable of binding to Nogo, MAG and/or TN-R, the method comprising:

providing bacteriophages of claim 61, expressing said fusion protein consisting of said at least one peptide; and  
screening the bacteriophages for the ability to bind to Nogo, MAG and/or TN-R.

64. (New) A composition comprising the vector of claim 38, formulated together with one or more pharmaceutically acceptable ingredients for use as a therapeutic vaccine, said composition optionally being formulated for injection.